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14. ABSTRACT

Major research accomplishment during the first year of this research project includes 1) fabrication of a fast speed noninvasive PAT prostate imaging system by using a stand-alone commercial ultrasound system; 2) testing the performance of this imaging system through the experiments on phantoms and ex vivo canine prostates; and 3) fabrication and optimization of a specially designed PVDF array transducer for high sensitive broad bandwidth detection of photoacoustic signals.

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INTRODUCTION

The ultimate goal of this research is to adapt spectroscopic photoacoustic tomography (SPAT) to prostate cancer imaging and evaluation, and fill the existing void in the early diagnosis, localization and accurate grading of prostate cancer, as well as in future treatment planning and therapeutic monitoring. As an essential step toward the ultimate goal, the objective of this funded project is to develop a laboratory prototype photoacoustic tomography (PAT) system that enables simultaneous photoacoustic and ultrasound imaging of prostates.

BODY

Task 1. Design and develop a noninvasive SPAT system with near-infrared (NIR) laser light and an ultrasonic transducer array for imaging prostates.

Task 1 has been completed. We have successfully achieved high speed SPAT using our z.one ultrasound (US) system from Zonare Medical Systems. As one of the research collaborators of Zonare, we have received strong technique support from them for the modification of the z.one to make it work on the SPAT mode. We have examined the performance of the z.one for SPAT by employing a commercial L10-5 or P4-1 probe from Zonare. With the 64 parallel acquisition channels of the z.one, this system has achieved real-time photoacoustic imaging with a frame rate of 10 Hz that is only limited by the laser repetition rate. Through this arrangement, SPAT takes the advantages from the state-of-the-art US image processing, management and display technologies without affecting the original imaging functions of the US system. A target prostate can now be scanned in both US and SPAT modes using the same acquisition system and through the same view angle, which facilitates off-line image co-registration and interpretation of SPAT outcomes.

As another essential development of the new SPAT system, we have fabricated and tested a specially designed PVDF array transducer through the collaboration with the researchers at the NIH Resource on Medical Ultrasonic Transducer Technology at the University of Southern California (USC). Unlike ordinary PZT transducers for US, this PVDF array enables both high receiving sensitivity and broad bandwidth. The researchers at USC have built three 128-channel receive-only arrays. Two of arrays were built using a 100 μm thick layer of co-polymer PVDF as the active material and a custom designed flexible circuit and printed circuit board connector for interconnect. According to our measurements, these two arrays enable a very broad receiving bandwidth of 125% which may significantly benefit photoacoustic imaging by enabling satisfactory spatial resolution. The third array incorporateing a 50-μm thick PVDF layer will be used to test our theory that an improved electrical impedance match to the receive preamplifiers will result in a larger signal-to-noise ratio (SNR). The researchers at USC have also fabricated a 16-channel preamplifier test-board. This board has been used to evaluate several commercial preamplifiers which are candidates for the ultimate 128-channel design. According to our measurements, this preamplifier can lead to 20 dB signal amplification with a satisfactory SNR. After testing on the 16-channel preamplifier board, the appropriate single channel preamplifier circuit design has been used in the layout of a 128-channel preamplifier board. In order to connect the array with the z.one, a customer designed cable has also been developed by Zonare. Now the researchers at Zonare are working on the software which will enable z.one to drive the customer designed PVDF array. We expect that, using the specially designed

PVDF array and the preamplifier board with a fixed gain of 20 dB and electrical impedance matching, this fast-speed SPAT acquisition system will present significantly improved performance in the proposed imaging experiments.

Task 2. Examine and optimize this imaging system through experiments on phantom samples.

Task 2 has been completed. To examine the performance of this imaging system, experiments have been conducted on micro-flow vessel phantoms and *ex vivo* fresh canine prostates. Preliminary results indicate that an object can be imaged in both US and SPAT modes, and that ultrasonic and optical contrast can be presented in a composite image display. In the SPAT images, vascular structures can be presented clearly and consistently with good contrast-to-noise ratio and satisfactory spatial resolution. Using the P4-1 probe which has a fairly broad -6 dB receiving bandwidth of 94 %, the axial and lateral resolution achieved by this system have been quantified as 0.65 mm and 0.88 mm respectively at the depth of 14 mm.

Using an ex vivo canine prostate model, the capability of this system in imaging of subsurface tissue inflammation or lesion has been explored. A lesion containing 50% of blood was induced at a depth of 1.5 cm in a canine prostate and then imaged by both SPAT and US. In SPAT images, the lesion can be visualized clearly based on the intrinsic optical contrast between the lesion and the background tissue. One of the main advantages of the US and SPAT dual-modality arrangement is the convenience in combining US and PAT results together for comprehensive diagnosis. In the combined result which is a SPAT image superimposed on the US image of the same prostate along the same view angle, we can clearly see the lesion and its relative position in the prostate. We have also explored the capability of SPAT in functional imaging of blood oxygenation. The maximum image intensity in the lesion area was stronger at 720-nm wavelength than that at 868-nm wavelength with a ratio of 1:0.6. With these image intensities at the two wavelengths measured, we have simulated the blood oxygenation level in the lesion which was 9 % and close to the 8 % oxygenation level measured by a blood gas analyzer. This match has indicated that SPAT may contribute to diagnostic imaging and therapeutic monitoring of prostate cancer by quantifying the regional hemoglobin oxygen saturation in the prostate tumor.

In this study, SPAT has presented unique advantages in mapping the blood vessels and the lesions with high blood content; while the tissue morphological features presented by US images has facilitated the interpretation of SPAT findings. Two papers associated with the above results have been reported in 2008 IEEE International Ultrasound Symposium and will appear soon in the conference proceeding. Another journal paper has been submitted to Ultrasound in Medicine & Biology.

In another study, we have discoverred for the first time that introducing of an optical contrast agent may significantly enhance SPAT performance by enabling truly quantitative measurement of subsurface tissue optical absorption spectrum. As a result, SPAT will be able to quantify hemodynamic activities in deep tissue without being affected by the strong light attenuation in the background. In SPAT, the intensity of photoacoustic signal induced by optical absorption in biological tissue is proportional to regional light energy deposition which is the product of the tissue optical absorption coefficient and the local light fluence. Because tissue optical properties are highly dependent on the wavelength, the spectrum of the local light fluence at a target tissue beneath the sample surface is different than the spectrum of the incident light fluence on the sample surface.

Therefore, quantifying tissue optical absorption spectrum by using photoacoustic technique is not feasible without the knowledge of the local light fluence. In our study, highly accurate photoacoustic measurement of subsurface tissue optical absorption spectrum has been realized for the first time by introducing an extrinsic optical contrast agent with known optical properties. From the photoacoustic measurements with and without the contrast agent, a differentiation imaging can be conducted and a quantified measurement of chromophore absorption spectrum can be achieved in a strongly scattering medium. Experiments on micro-flow vessels containing fresh canine blood buried in tissue-mimicking phantoms and chicken breast tissues were carried out in a wavelength range from 680 nm to 950 nm. Spectroscopic photoacoustic measurements of both oxygenated and deoxygenated blood specimens have presented clearly improved match with the gold standard when employing this new technique.

One papers associated with the above study has been reported in 2009 SPIE Photonics West: BIOS conference and will appear soon in the conference proceeding. Another journal paper has been accepted by Optics Express. In the future, we will continue the validation and development of this novel technique through the study on living animals. Moreover, feasibility of SPAT aided by a variety of optical contrast agents including metallic nanocolloids and organic dyes will be examined.

Task 3 and 4. ***Validate the performance of this system for photoacoustic and ultrasound imaging of normal canine prostates; and explore the sensitivity of this system in detection regional hemodynamic changes in canine prostates, including blood oxygen saturation and blood volume.***

Task 3 and 4 are on going. According to the specific aims of this project, we will get a specially designed transducer probe for SPAT of prostate from the University of Southern California (USC) by the end of year 1 (Feb. 2008). However, the fabrication of this transducer was significantly delayed due to some unexpected technical difficulties. The transducer probe and the preamplifier board have been delivered to our group in Dec. 2008. We are now conducting the proposed experiments on animals and will need more time to finish. Therefore, we have applied for 1 year extension of this project with no additional cost. The final report will be submitted by March 15, 2010.

KEY RESEARCH ACCOMPLISHMENTS

1) Complete the adaptation of the z.one commercial US system for high-speed noninvasive photoacoustic imaging. Complete the fabrication and optimization of a specially designed PVDF array transducer for enhanced SPAT imaging of prostate cancer.

2) Through the experiments on phantoms and ex vivo canine prostate specimens, test and validate the good performance of this SPAT and US dual-modality imaging system for describing vascularity and subsurface lesions.

3) Develop a novel differentiation SPAT technique by using optical contrast agents for truly quantitative evaluation of subsurface tissue optical absorption spectrum and hemodynamic properties including both blood oxygenation and blood volume.

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CONCLUSION

During the past two years, we have finished the fabrication and testing of a fast speed noninvasive SPAT prostate imaging system by using a stand-alone US machine and a tunable pulsed laser. The good performance of this system has been validated through the experiments on phantoms and ex vivo canine prostates. We have also developed a novel technique for SPAT to quantify the spectroscopic tissue optical absorption in a highly scattering medium by using extrinsic optical contrast agents. Preliminary studies on phantoms and *ex vivo* chicken breast tissues have proven the feasibility of this method. Several papers have been published or accepted from these works. At the same time, a specially designed PVDF array probe and a 128-channel preamplifier board have also been developed. By using this array probe for signal receiving instead of commercial ultrasound probes, we expect significantly improved sensitivity and image quality for SPAT of prostate cancer.